

**ESTER DERIVATIVES****Publication number:** WO0204402**Publication date:** 2002-01-17**Inventor:** OGINO YOSHIO (JP); KURIHARA HIDEKI (JP);  
MATSUDA KENJI (JP); NUMAZAWA TOMOSHIGE (JP);  
OTAKE NORIKAZU (JP); NOGUCHI KAZUHITO (JP)**Applicant:** BANYU PHARMA CO LTD (JP); OGINO YOSHIO (JP);  
KURIHARA HIDEKI (JP); MATSUDA KENJI (JP);  
NUMAZAWA TOMOSHIGE (JP); Otake NORIKAZU  
(JP); NOGUCHI KAZUHITO (JP)**Classification:**

**- international:** A61P11/00; A61P11/06; A61P27/16; A61P43/00;  
C07C219/10; C07C219/14; C07D205/04; C07D207/08;  
C07D207/12; C07D209/52; C07D211/22; C07D211/42;  
C07D211/46; C07D211/70; C07D239/06; C07D451/02;  
C07D451/06; C07D471/08; C07D471/10; C07D487/10;  
C07D498/10; A61P11/00; A61P27/00; A61P43/00;  
C07C219/00; C07D205/00; C07D207/00; C07D209/00;  
C07D211/00; C07D239/00; C07D451/00; C07D471/00;  
C07D487/00; C07D498/00; (IPC1-7): C07C219/10;  
A61K31/222; A61K31/395; A61K31/397; A61K31/40;  
A61K31/403; A61K31/407; A61K31/435; A61K31/438;  
A61K31/439; A61K31/4409; A61K31/452; A61K31/4525;  
A61K31/5386; A61K31/55; A61P11/00; A61P11/06;  
A61P27/16; A61P43/00; C07C219/22; C07C219/24;  
C07C251/08; C07C251/18; C07D205/04; C07D207/08;  
C07D207/12; C07D209/52; C07D211/22; C07D211/46;  
C07D211/70; C07D221/24; C07D239/06; C07D295/125;  
C07D405/12; C07D451/02; C07D471/10; C07D487/10;  
C07D498/10

**- european:** C07C219/10; C07C219/14; C07D205/04; C07D207/08A;  
C07D207/12; C07D209/52; C07D211/22; C07D211/42;  
C07D211/46; C07D211/70; C07D239/06B3;  
C07D239/06C; C07D451/02B; C07D451/06D;  
C07D471/08; C07D471/10; C07D487/10; C07D498/10

**Application number:** WO2001JP05987 20010710**Priority number(s):** JP20000210591 20000711**Also published as:**

EP1302458 (A1)  
US6846835 (B2)  
US2003191316 (A1)  
CA2415468 (A1)

attached

**Cited documents:**

WO9821183  
EP0140434  
FR1352332

**Report a data error here****Abstract of WO0204402**

Compounds of the general formula (I), which exhibit selective muscarinic M3 receptor antagonism, little have side effects, and are suitable for administration by inhalation and useful as therapeutic agents for respiratory system diseases or the like: (I) wherein A is a group of the general formula (a0) or (b0): (a0) (b0) Ar is aryl or heteroaryl, any of which may be substituted; B<1> and B<2> are each an aliphatic hydrocarbon group; R<1> is fluorinated cycloalkyl; R<2>, R<3> and R<4> are each lower alkyl, or a single bond or alkylene, any of which is bonded to B<1>, or alternatively R<2> and R<3> may be united to form alkylene; R<5> and R<7> are each hydrogen, lower alkyl, or a single bond or alkylene, any of which is bonded to B<2>; R<6> is hydrogen, lower alkyl, or N(R<8>)R<9>; and X<-> is an anion.

Compounds of the general formula (I), which exhibit selective muscarinic M3 receptor antagonism, little have side effects, and are suitable for administration by inhalation and useful as therapeutic agents for respiratory system diseases or the like: (I) wherein A is a group of the general formula (a0) or (b0): (a0) (b0) Ar is aryl or heteroaryl, any of which may be substituted; B<1> and B<2> are each an aliphatic hydrocarbon group; R<1> is fluorinated cycloalkyl; R<2>, R<3> and R<4> are each lower alkyl, or a single bond or alkylene, any of which is bonded to B<1>, or alternatively R<2> and R<3> may be united to form alkylene; R<5> and R<7> are each hydrogen, lower alkyl, or a single bond or alkylene, any of which is

bonded to B<2>; R<6> is hydrogen, lower alkyl, or N(R<8>)R<9>; and X<-> is an anion.

---

Data supplied from the **esp@cenet** database - Worldwide



US006846835B2

(12) **United States Patent**  
Ogino et al.

(10) **Patent No.:** US 6,846,835 B2  
(45) **Date of Patent:** Jan. 25, 2005

(54) **ESTER DERIVATIVES**

(75) **Inventors:** Yoshio Ogino, Tsukuba (JP); Hideki Kurihara, Tsukuba (JP); Kenji Matsuda, Tsukuba (JP); Tomoshige Numazawa, Tsukuba (JP); Norikazu Otake, Tsukuba (JP); Kazuhito Noguchi, Tsukuba (JP)

(73) **Assignee:** Banyu Pharmaceutical Co., Ltd., Tokyo (JP)

(\*) **Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) **Appl. No.:** 10/332,617

(22) **PCT Filed:** Jul. 10, 2001

(86) **PCT No.:** PCT/JP01/05987

§ 371 (c)(1),  
(2), (4) **Date:** Jan. 10, 2003

(87) **PCT Pub. No.:** WO02/04402

**PCT Pub. Date:** Jan. 17, 2002

(65) **Prior Publication Data**

US 2003/0191316 A1 Oct. 9, 2003

(30) **Foreign Application Priority Data**

Jul. 11, 2000 (JP) ..... 2000-210591

(51) **Int. Cl.<sup>7</sup>** ..... A61K 31/445; A61K 31/4465; C07D 221/02; C07D 211/04

(52) **U.S. Cl.** ..... 514/317; 514/318; 546/192; 546/194; 546/236

(58) **Field of Search** ..... 546/192, 194, 546/236; 514/317, 318

(56) **References Cited****U.S. PATENT DOCUMENTS**

3,903,094 A \* 9/1975 Witten et al. .... 546/204  
6,482,837 B1 \* 11/2002 Wood ..... 514/315  
6,484,837 B1 \* 11/2002 Buell et al. .... 180/225

**FOREIGN PATENT DOCUMENTS**

EP ..... 140434 ..... 5/1985  
EP ..... 0 309 424 ..... 3/1989  
FR ..... 1352332 ..... 1/1964  
JP ..... 1-131145 ..... 5/1989  
WO ..... 98/21183 ..... 5/1998

**OTHER PUBLICATIONS**

V. Tumietti et al., "Affinity and selectivity at M<sub>2</sub> and M<sub>3</sub> muscarinic receptor subtypes of cyclic and open oxygenated analogues of 4-DAMP (\*)", *Farmaco*, vol. 47, No. 9, pp. 1133-1147, 1992.

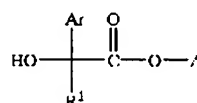
\* cited by examiner

*Primary Examiner*—Rita Desai

(74) *Attorney, Agent, or Firm*—Wenderoth, Lind & Ponack, L.L.P.

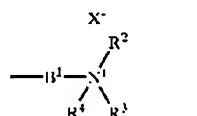
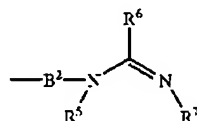
(57) **ABSTRACT**

This invention relates to compounds which exhibit selective muscarinic M<sub>3</sub> receptor antagonism, have little side effects, are suitable for inhalation therapy and are useful as treating agents of respiratory system diseases, of the general formula (I);



(I)

[in which A signifies a group expressed by a formula (a<sub>0</sub>) or (b<sub>0</sub>);

(a<sub>0</sub>)(b<sub>0</sub>)

Ar signifies optionally substituted aryl or heteroaryl; B<sup>1</sup> and B<sup>2</sup> signify aliphatic hydrocarbon; R<sup>1</sup> signifies fluorine-substituted cycloalkyl; R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> signify lower alkyl, single bond or alkylene bonded to B<sup>1</sup>, or R<sup>2</sup> and R<sup>3</sup> are united to signify alkylene; R<sup>5</sup> and R<sup>7</sup> signify hydrogen, lower alkyl, or a single bond or alkylene bonded to B<sup>2</sup>; R<sup>6</sup> signifies hydrogen, lower alkyl or a group expressed as  $\text{---N(R}^6\text{)R}^6$ ; and X<sup>-</sup> signifies an anion].

**32 Claims, No Drawings**